# CLAIMS

We claim,

1. A method of identifying a site of interaction between a first and second macromolecule, comprising:

   (a) immobilizing the first macromolecule onto at least two biosensor surfaces;

   (b) treating each biosensor surface containing the immobilized first macromolecule with a different agent capable of altering the structure of the immobilized first macromolecule;

   (c) exposing each treated biosensor surface to the second macromolecule;

   (d) determining an interaction profile of the second macromolecule to the immobilized and treated first macromolecule; and

   (e) identifying a site of interaction between the first and second macromolecules based on the interaction profile.

2. The method of claim 1, wherein the agent capable of altering the structure of the first macromolecule is an enzyme.

3. The method of claim 2, wherein the enzyme is a proteolytic enzyme.

4. The method of claim 3, wherein the proteolytic enzyme is selected from the group consisting of trypsin, endoproteinase Glu-C, endoproteinase Asp-N, chymotrypsin, endoproteinase Lys-C, and endoproteinase Arg-C.

5. The method of claim 2, wherein the enzyme is selected from the group consisting of a lipase, amylase, and endonuclease.

6. The method of claim 1, wherein the agent capable of altering the structure of the first macromolecule is a chemical agent.

7. The method of claim 6, wherein the chemical agent is selected from the group consisting of Tris (2-carboxyethyl) phosphine hydrochloride (TCEP•HCl), N-ethyl-N'-(dimethylaminopropyl) carbodiimide (EDC), iodoacetamide, hydrazine, p-hydroxyphenylglyoxal (HPG), hydrogen peroxide, N-bromosuccinimide, N-acetylimidazole, tetranitromethane, arsanilic acid, dansyl chloride, glutaraldehyde, ninhydrin, and diethylpyrocarbonate (DEPC).

8. The method of claim 6, wherein the first macromolecule is a lipid and the chemical agent is selected from the group consisting of reactive compounds that modify lipids by N-ethyl-N'-

20

(dimethylaminopropyl) carbodiimide (EDC)-mediated chemistry.

9. The method of claim 6, wherein the first macromolecule is a carbohydrate and the chemical agent is selected from the group consisting of primary amine-containing compounds that modify carbohydrates by periodate-mediated chemistry.

10. The method of claim 6, wherein the first macromolecule is a nucleic acid and the chemical agent is a methylating agent.

11. The method of claim 1, wherein the biosensor surface is a Biacore biosensor surface.

12. The method of claim 1, wherein the biosensor surface is an IAsys® biosensor surface, a SPR670 biosensor surface, a Bio-Suplar II biosensor surface, or a Spreeta™ biosensor surface.

13. The method of claim 1, wherein the first macromolecule and the second macromolecule are selected from the group consisting of:
     (a) proteins, wherein the proteins are different proteins;
     (b) a protein and a carbohydrate;
     (c) a protein and a ligand;
     (d) a protein and a nucleic acid; and
     (e) a ligand and a receptor.

14. The method of claim 13, wherein the ligand is selected from the group consisting of a carbohydrate, nucleic acid, small molecule, peptide, and lipid.

15. The method of claim 14, wherein the nucleic acid is DNA or RNA.

16. The method of claim 13, wherein the protein is a transcription factor.

17. A method of sorting antigen-specific monoclonal antibodies (mAbs) into functional groups, comprising:
     (a) immobilizing the antigen onto at least two biosensor surfaces;
     (b) treating each biosensor surface with a different agent, wherein each agent is capable of altering the structure of the immobilized antigen;
     (c) exposing each treated biosensor surface to the antigen-specific mAbs;
     (d) determining the binding profile of the monoclonal antibodies to each treated biosensor surface; and

21

(e) sorting the mAbs into functional groups based on a binding profile of the monoclonal antibodies to each treated biosensor surface, wherein mAbs that exhibit similar binding profiles to each treated sensor surface are sorted into the same functional group.

18. The method of claim 17, wherein the agents capable of altering the structure of the immobilized antigen are enzymes.

19. The method of claim 18, wherein the enzymes are proteolytic enzymes selected from the group consisting of trypsin, endoproteinase Glu-C, endoproteinase Asp-N, chymotrypsin, endoproteinase Lys-C, and endoproteinase Arg-C.

20. The method of claim 17, wherein the agents capable of altering the structure of the immobilized antigen are chemical agents selected from the group consisting of Tris (2-carboxyethyl) phosphine hydrochloride (TCEP•HCl), N-ethyl-N'-(dimethylaminopropyl) carbodiimide (EDC), iodoacetamide, hydrazine, p-hydroxyphenylglyoxal (HPG), hydrogen peroxide, N-bromosuccinimide, N-acetylimidazole, tetranitromethane, arsanilic acid, dansyl chloride, glutaraldehyde, ninhydrin, and diethylpyrocarbonate (DEPC).

21. The method of claim 17, wherein the biosensor surface is a Biacore sensor surface an IAsys® biosensor surface, a SPR670 biosensor surface, a Bio-Suplar II biosensor surface, or a Spreeta™ biosensor surface.